

**AMENDMENTS TO THE SPECIFICATION**

Please replace the paragraph beginning at page 27, line 3, with the following amended paragraph:

In order to determine whether the histidine copolymer is physically linked to the liposome: DNA complex, the ~~effects~~ effect on transfection efficiency was examined after varying the order of addition of these three components. When the polymer was first incubated with the DNA, and then mixed with the liposomes, the greatest enhancement of transfection efficiency ( $p < 0.05$ ) (Figure 7). With all other mixing permutations, the transfection efficiency with H-K was reduced. Lesser transfection efficiency occurred when liposomes were first incubated with plasmid DNA, and later the polymer was added. Intermediate reductions in transfection occurred when the liposomes and polymer were simultaneously added to plasmid DNA. Similar results occurred with or without serum. Unless the polymer is first mixed with the DNA, the low molecular weight polymer may not be able to compete adequately with the cationic liposomes for the negatively charged plasmid DNA. Although enhancement of transfection efficiency has been reported to occur as a result of interaction of cationic polymers with inhibitory proteins in the serum (9), pre-mixing the histidine copolymer with serum did not enhance the transfection efficiency of the liposome: DNA complex (data not shown). These findings suggest that the polymer is integrated into the liposome: DNA complex, and this tripartite complex is important for increased transfection efficiency.

Please replace the paragraph beginning at page 29, line 8, with the following amended paragraph:

The sequence order of the H-K amino acids can affect transfection efficiency. Polymers H-K, Y-HK (SEQ ID NO:7), and Y-HH (SEQ ID NO:8) were mixed initially with DNA and then liposomes were added as previously described. While all accelerated useful transfection efficiency, the Y-HH polymer significantly enhanced the uptake of liposomes in the presence or absence of serum (Figure 13). Since the Y peptide component (Y-G-R-K-K-R-R-Q-R-R-R) (SEQ ID NO:17) was present in both the Y-HK and the Y-HH polymers, the critical sequence that enhanced uptake in the Y-HH polymer was the HH component (H-H-K-H-H-K-H-H-K-H-H-K-H-H-K) (SEQ ID NO:15). For this reason, the latter sequence is a currently preferred embodiment of the invention.

Please replace the section heading at page 29, line 31, with the following amended heading:

**6.4.12 Comparison of H-K2b:Liposome Carriers ~~H-K2b in Combination of Liposomes with PEI.~~**

Please replace the paragraph beginning at page 30, line 27, with the following amended paragraph:

***In vivo* delivery of pharmaceutical agents.** The following example demonstrates that HH-K4b has utility *in vivo* as a carrier of low molecular weight DNA molecules in the absence of an intracellular delivery compound. In this example, the receptor of VEGF mRNA with a DNA oligonucleotide that has enzymatic activity (also called DNAzyme) (36) was targeted. The VEGF receptor is essential for tumor angiogenesis and consequently tumor growth. After breast cancer cells (MDA-MB-435 cells) were injected into nude mice and the tumors grew to a visible size, the tumor was injected with the therapeutic polymer-DNA complex. The tumor was injected every 5 days for a total of 5 injections. There were 4 treatment groups: 1) untreated, 2) HH-K4B carrier alone, 3) HH-K4b + DNAzyme, and 4) HH-K4b + antisense oligonucleotides. To prepare the complex for injection, 45 µg of the HH-K4b polymer diluted in 150 µl of water was mixed with 24 µg of oligonucleotide, also diluted in 150 µl of water. After formation of the complex for 2 hours, 25 µl of the treatment complex was injected into each tumor. The therapeutic oligonucleotide sequence is 5'-TGCTCTCCA-GGCTAGCTACAACGA-CCTGCACCT-3' (SEQ ID NO:18) whereas the control antisense oligonucleotide sequence is 5'-TGCTCTCCA-GGCTATGTACAACGA-CCTGCACCT-3' (SEQ ID NO:19). The only difference between the therapeutic DNAzyme sequence and the antisense sequences is that the nucleotides responsible for cleaving the mRNA have been altered with the antisense DNA. The tumor volume, measured before each injection, is given in the table below.

Please substitute the current paper copy of the "Sequence Listing" with the attached paper copy of the "Sequence Listing."